Strategic Pathways for AI-Enabled Phytopharmaceutical Translation: Data Infrastructure, Model Validation, Mechanistic Evidence, Regulatory Alignment, and Clinical Adoption

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ABSTRACT

AI-enabled phytopharmaceutical translation is emerging at the intersection of natural product research, computational pharmacology, translational science, regulatory interpretation, and responsible clinical innovation. Although artificial intelligence may support compound prioritisation, target prediction, evidence integration, and safety-aware hypothesis generation, translation requires more than predictive performance. This original strategic roadmap article proposes a staged framework for moving AI-enabled phytopharmaceutical evidence from discovery-oriented outputs toward responsible translational planning. The roadmap emphasises interoperable data infrastructure, FAIR chemical and biological records, provenance, natural product identity, chemical annotation, bioactivity evidence, safety data, and clinical evidence traceability. It further defines model validation requirements, including internal testing, external validation, benchmarking, uncertainty communication, explainability, bias assessment, and generalisability. Mechanistic evidence is positioned as a plausibility layer requiring target evidence, pathway evidence, experimental validation, exposure relevance, ADMET interpretation, and safety validation, while regulatory alignment is framed as evidence-to-claim mapping rather than approval. Clinical adoption is treated as a later-stage pathway requiring workflow fit, clinician trust, human oversight, patient safety safeguards, implementation monitoring, and pharmacovigilance readiness. The main contribution is a structured strategic roadmap that links data readiness, model credibility, mechanistic plausibility, safety interpretation, regulatory logic, clinical workflow integration, governance safeguards, and continuous evidence updating while avoiding claims of clinical readiness without appropriate validation.

Key Words: *AI-enabled phytopharmaceuticals, Translation, Aata infrastructure, Model validation, Mechanistic evidence, Regulatory alignment*

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INTRODUCTION

Artificial intelligence has become a prominent methodological layer in drug discovery, supporting tasks such as compound prioritisation, property prediction, target inference, molecular design, and evidence integration. For phytopharmaceutical translation, however, AI must be understood as part of a broader translational pathway rather than as an autonomous route from prediction to clinical use. Machine learning can strengthen

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discovery workflows when models are trained, evaluated, interpreted, and updated within transparent evidence systems, but predictive outputs remain conditional on the quality, representativeness, and biological relevance of the data from which they are derived [1].

The strategic challenge is especially clear in AI-enabled phytopharmaceutical research because the development pathway involves heterogeneous compounds, complex extracts, traditional-use contexts, multi-target pharmacology, variable chemical annotation, and fragmented safety evidence. AI methods may assist discovery and development by linking chemical, biological, pharmacological, and literature-derived evidence, but each output requires interpretation according to its intended translational role. A model trained for prioritisation cannot be treated as a validated clinical decision-support tool, and an internal prediction cannot be equated with external validity, prospective performance, experimental confirmation, or clinical utility [2].

Natural product research adds further complexity because phytopharmaceutical candidates often arise from chemically diverse sources, variable extraction conditions, incomplete structural annotation, and context-dependent bioactivity data. The translation of natural product evidence therefore requires a layered framework in which identity, provenance, bioactivity, mechanism, safety, formulation context, and clinical evidence are connected rather than evaluated as isolated data points. Without such integration, AI-enabled prioritisation may amplify uncertainty by treating incomplete or weakly annotated natural product records as if they were standardised pharmaceutical entities [3].

A strategic roadmap is therefore needed to define how AI-enabled phytopharmaceutical evidence should progress from discovery-stage hypotheses to translation planning. This article proposes such a roadmap by linking data infrastructure, model validation, mechanistic evidence, safety interpretation, regulatory alignment, clinical adoption planning, governance safeguards, and continuous evidence updating. The aim is not to present an implemented platform, clinical guideline, regulatory pathway, or validated decision-support system, but to define a staged translational logic in which computational hypotheses are progressively constrained by evidence quality, validation requirements, claim boundaries, and human oversight [4].

AI-enabled phytopharmaceutical translation

AI-enabled phytopharmaceutical translation can be conceptualised as a staged process that begins with discovery-oriented computational outputs and progresses only when additional evidence supports credibility, plausibility, safety, and appropriate use boundaries. In this context, AI may help connect phytochemical profiles, target hypotheses, omics patterns, pharmacological annotations, toxicity signals, and clinical evidence fragments. Yet the translational value of these connections depends on whether the underlying data are traceable, whether the model has been evaluated beyond its development setting, and whether the output is positioned as hypothesis generation rather than clinical instruction [5].

The complexity of natural products makes this staged interpretation essential. Phytopharmaceutical candidates may include purified compounds, enriched fractions, standardised extracts, or multi-component preparations, each with different requirements for identity, reproducibility, mechanism, and safety interpretation. AI can support prioritisation by searching chemical space, identifying similarity patterns, predicting bioactivity, and ranking candidates for further investigation, but these functions remain bounded by annotation quality, assay comparability, dataset completeness, and model generalisability [6].

AI-enabled phytopharmaceutical translation also benefits from the integration of genomics, biosynthetic evidence, metabolomics, and other omics-linked data streams. These data can help connect natural product diversity with chemical families, biosynthetic origins, biological targets, and therapeutic plausibility. However, omics-informed inference does not automatically establish efficacy or safety; it instead provides a richer evidence layer for prioritising experimental validation, refining mechanism hypotheses, and assessing whether predicted effects are biologically coherent within disease-relevant contexts [7].

Natural product informatics can support this translation pathway by organising chemical, taxonomic, pharmacological, and literature-derived records into computationally usable structures. Still, automation and informatics should not be treated as substitutes for experimental testing, regulatory interpretation, clinical judgment, or safety governance. Automated discovery systems can accelerate search and ranking, but the translation of phytopharmaceutical evidence requires explicit claim boundaries, uncertainty communication, stakeholder trust, and review points where computational outputs are checked against biological, safety, regulatory, and clinical constraints [8]. Automated drug discovery therefore provides a useful technological direction while reinforcing the need for validation, interpretability, and staged decision-making [9].

Data infrastructure and model validation

Data infrastructure is the foundation of responsible AI-enabled phytopharmaceutical translation. For chemical evidence, FAIR representation requires that structures, identifiers, stereochemical information, source context,

and metadata be findable, accessible, interoperable, and reusable. In phytopharmaceutical research, this requirement is not a technical formality; it determines whether compounds, extracts, assays, and safety signals can be traced, compared, linked, and reanalysed across studies. FAIR chemical structures therefore support translation by reducing ambiguity in compound identity and enabling reproducible downstream modelling [10]. Open natural product collections further support this foundation by making chemical diversity more visible, but database inclusion alone does not establish biological validity or clinical relevance [11].

Provenance and interoperability are equally important because natural product evidence often crosses taxonomic, chemical, pharmacological, and literature-derived domains. Open knowledge-management approaches can improve traceability by linking natural products to sources, identifiers, annotations, and contextual metadata, thereby helping AI systems distinguish between well-characterised records and weakly supported entries [12]. Activity and species-source databases add another critical layer by connecting natural products to reported biological activities and organismal origins, but such records still require careful interpretation because assay conditions, potency measures, extract composition, and experimental comparability may vary across studies [13].

Model validation must be treated as a sequence of credibility checks rather than a single performance estimate. Internal validation may show that a model performs on held-out data from a development set, but it does not necessarily show that the model will generalise across new chemical scaffolds, different natural product classes, independent assay systems, or clinically relevant populations. Benchmarking resources in molecular machine learning demonstrate the importance of standardised datasets and evaluation procedures, while also highlighting the risk that benchmark performance can overstate translational readiness when dataset shift, leakage, limited chemical diversity, or weak external testing are not addressed [14].

Explainability and safety-aware prediction should be integrated into model validation rather than added as decorative features after model development. Explainable AI may help researchers inspect which chemical features, target associations, or pathway patterns contribute to a prediction, but explanations remain model-dependent and must not be treated as proof of mechanism [15]. ADMET prediction can support early safety-aware prioritisation by flagging absorption, distribution, metabolism, excretion, and toxicity concerns, yet in silico safety outputs require validation, uncertainty communication, and integration with experimental and pharmacovigilance evidence before they can support translational claims [16].

Table 1 summarises data infrastructure and model validation requirements for AI-enabled phytopharmaceutical translation.

Table 1. Data Infrastructure and Model Validation Requirements for AI-Enabled Phytopharmaceutical Translation: FAIR Data, Provenance, Interoperability, Chemical Annotation, Bioactivity Evidence, Safety Data, Model Validation, External Testing, Generalizability, and Uncertainty Reporting

Translation requirement	Core question	Required evidence or infrastructure	AI relevance	Validation need	Governance need	Failure risk	Roadmap role
FAIR chemical data	Are compounds and phytochemical entities represented in reusable form?	Standardised identifiers, structures, stereochemistry, source metadata, versioned records	Enables model-ready chemical inputs	Chemical-identity verification	Metadata stewardship	Misidentified or duplicated compounds	Foundational data-readiness gate
Data provenance	Can each record be traced to its source and context?	Source organism, extraction context, assay origin, curation history, record version	Supports trust in training and inference data	Provenance audit	Curation accountability	Untraceable evidence chains	Traceability layer
Data interoperability	Can chemical, biological, omics, safety, and clinical records be linked?	Shared identifiers, controlled vocabularies, harmonised metadata	Enables multimodal evidence integration	Cross-database consistency checks	Interoperability governance	Fragmented or incompatible datasets	Integration layer
Natural product identity	Is the phytopharmaceutical entity sufficiently defined?	Compound, fraction, extract, formulation, taxonomic, and preparation details	Prevents ambiguous model inputs	Identity confirmation	Source and preparation documentation	Treating non-equivalent entities as identical	Identity-control gate

Chemical annotation	Are chemical features sufficiently resolved for modelling?	Structural annotation, feature descriptors, confidence levels	Supports prediction and similarity analysis	Annotation-quality review	Annotation standards	Weak or erroneous chemical features	Model-input quality layer
Bioactivity evidence	Are biological effects linked to assay context?	Assay type, endpoint, potency, concentration, cell or target context	Supports activity prediction and prioritisation	Assay comparability review	Evidence grading	Overgeneralised bioactivity claims	Biological evidence layer
Safety data	Are toxicity, ADMET, and interaction risks captured?	ADMET data, toxicity signals, interaction records, exposure context	Supports safety-aware screening	Safety model validation	Safety escalation rules	Missed toxicity or interaction risk	Safety-readiness gate
Omics data	Are molecular response profiles available and interpretable?	Transcriptomic, proteomic, metabolomic, or single-cell evidence where relevant	Supports mechanism inference	Biological plausibility review	Omics data governance	Mechanistic overinterpretation	Mechanism-support layer
Clinical evidence data	Are human evidence records linked to claims and safety context?	Clinical study data, adverse-event records, population context, endpoints	Supports later translation planning	Clinical relevance review	Human evidence governance	Premature clinical inference	Clinical-evidence linkage
Internal validation	Does the model perform within development data?	Hold-out sets, cross-validation, calibration, appropriate metrics	Provides early technical credibility	Internal performance audit	Transparent reporting	Overfitting	Early model-credibility gate
External testing	Does the model generalise beyond development data?	Independent datasets, new chemical classes, different assay contexts	Tests model transportability	External validation	Independent review	Poor generalisability	Translation-credibility gate
Uncertainty reporting	Are prediction limits communicated?	Confidence intervals, calibration, uncertainty scores, applicability domain	Supports cautious interpretation	Uncertainty assessment	User-facing transparency	Overconfident decisions	Interpretation boundary
Bias assessment	Are dataset and model biases identified?	Dataset composition review, class imbalance checks, leakage assessment	Reduces misleading model behaviour	Bias and leakage evaluation	Bias governance	Systematic error propagation	Risk-control layer
Versioning and updating	Are datasets and models controlled over time?	Version histories, update triggers, change logs, revalidation plans	Enables reproducible and adaptive systems	Revalidation after updates	Change-control governance	Silent drift or uncontrolled updates	Lifecycle-management layer

Mechanistic evidence and regulatory alignment

Mechanistic evidence is a central bridge between AI-generated phytopharmaceutical hypotheses and responsible translation planning. Network pharmacology can help organise herbal and natural product evidence by linking compounds, predicted targets, pathways, and disease mechanisms, but network-derived associations should be interpreted as structured hypotheses rather than proof of therapeutic action [17]. Medicinal plant network models can clarify potential multi-target and pathway-level effects, yet their evidentiary strength depends on the quality of input data, the biological relevance of target mappings, and the availability of experimental validation that tests whether predicted mechanisms are observable under relevant pharmacological conditions [18].

Mechanistic plausibility can be strengthened when target evidence is connected to omics-informed biological context. Single-cell and multiomics approaches may refine

target identification by showing how natural product-related mechanisms align with disease-relevant cellular states, pathway dependencies, or molecular response profiles [19]. Metabolomics and genomics can also support natural product discovery by linking chemical entities, biosynthetic context, and biological activity, thereby improving the evidence chain between compound identity and functional interpretation [20]. Nevertheless, omics-supported plausibility remains a preclinical evidence layer unless supported by appropriate experimental, safety, and clinical evidence.

Regulatory alignment should be understood as the structured matching of evidence, intended use, claim type, documentation, validation level, uncertainty, and safety controls. Validation principles for AI-containing products across regulated healthcare contexts emphasise lifecycle evaluation, documentation, and the need to address performance across intended-use conditions rather than relying on isolated development results [21]. For AI-enabled phytopharmaceutical translation, this implies that discovery-stage predictions, externally validated models, mechanistic evidence, safety evidence, clinical evidence, and decision-support claims must be separated rather than collapsed into a single claim of readiness.

Regulatory evidence landscapes for AI and machine-learning-based medical technologies further illustrate the difference between evidence alignment and approval. Comparative analyses of AI/ML medical device approvals show that regulatory pathways require defined intended uses, evidence documentation, and boundaries of application, while approval status cannot be inferred from discovery evidence alone [22]. Databases of authorised AI-based medical devices and algorithms also show the importance of transparent reporting and defined use contexts when AI outputs enter regulated healthcare environments [23]. At the same time, algorithmic fairness and bias mitigation remain governance issues that cannot be solved solely through technical correction; responsible translation requires human oversight, safety review, accountability, and explicit acknowledgement of unresolved uncertainty [24].

Table 2 maps mechanistic evidence and regulatory alignment requirements for responsible phytopharmaceutical translation.

Table 2. Mechanistic Evidence and Regulatory Alignment for AI-Enabled Phytopharmaceutical Translation: Target Evidence, Pathway Evidence, Experimental Validation, Safety Evidence, Claim Boundaries, Evidence Standards, Regulatory Interpretation, and Validation Gaps

Evidence or alignment domain	Core translational question	Evidence needed	Regulatory relevance	Interpretation boundary	Validation requirement	Risk of overclaiming	Strategic implication
Target evidence	Are predicted targets biologically relevant?	Target prediction, literature support, binding or activity evidence, disease relevance	Supports claim-specific biological rationale	Target association is not therapeutic proof	Independent target validation	Claiming mechanism from prediction alone	Use as mechanism-hypothesis layer
Pathway evidence	Are pathways plausibly affected in disease-relevant contexts?	Pathway enrichment, omics response, disease biology linkage	Helps define mechanistic plausibility	Pathway mapping does not establish efficacy	Experimental or omics validation	Overstating network associations	Connect mechanism to testable biology
Network pharmacology	Are compound-target-pathway relationships coherent?	Curated compound, target, pathway, and disease networks	Supports evidence organisation	Network topology is not validation	Input-quality and biological review	Treating network diagrams as causal proof	Use for structured hypothesis generation
Experimental validation	Are computational predictions observed experimentally?	Biochemical, cellular, omics, pharmacological, or safety assays	Strengthens evidence package	Preclinical validation is not clinical utility	Reproducible assay design	Generalising from limited assays	Evidence-strengthening gate
Exposure plausibility	Can predicted effects occur at relevant exposure levels?	Concentration, bioavailability, metabolism, tissue exposure, formulation context	Supports claim realism	In vitro activity may not translate in vivo	Pharmacokinetic and exposure assessment	Ignoring achievable exposure	Translation plausibility checkpoint

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Safety validation	Are toxicity and interaction risks evaluated?	ADMET, toxicity, interaction, contraindication, and safety signal evidence	Central to risk-benefit interpretation	Safety prediction is not safety assurance	Experimental and clinical safety review where relevant	Assuming natural origin implies safety	Safety-readiness gate
Pharmacovigilance evidence	Can post-use safety signals be detected and interpreted?	Adverse-event reports, exposure context, interaction signals, signal-detection plan	Supports lifecycle safety monitoring	Signal readiness is not evidence of safety	Pharmacovigilance workflow assessment	Missing delayed or rare harms	Monitoring and feedback layer
Claim boundaries	What can be claimed from current evidence?	Evidence-to-claim mapping, uncertainty statement, intended-use definition	Prevents unsupported translational claims	Claim wording must match evidence level	Claim audit	Presenting discovery evidence as clinical evidence	Strategic claim-control tool
Evidence standards	What evidence is sufficient for each translation stage?	Data, model, mechanism, safety, and clinical evidence standards	Supports regulatory interpretation	Standards guide but do not guarantee approval	Evidence-quality review	Confusing alignment with acceptance	Evidence-threshold framework
Regulatory interpretation	Which pathway or review logic may be relevant?	Intended use, risk context, documentation, validation, safety evidence	Frames regulatory readiness	Interpretation is not regulatory approval	Expert regulatory review	Implying authority endorsement	Regulatory planning layer
Validation gaps	What evidence is still missing?	Gap analysis across data, model, mechanism, safety, clinical, and workflow domains	Identifies limits of claims	Gap recognition is not readiness	Gap-specific validation plan	Hiding uncertainty	Translation-risk reduction
Uncertainty communication	Are limitations visible to users and reviewers?	Applicability domains, confidence, unresolved evidence gaps, bias statement	Supports transparent review	Communication does not remove uncertainty	User-facing and reviewer-facing testing	Overconfidence in model outputs	Trust and governance safeguard

Clinical adoption pathways

Clinical adoption of AI-enabled phytopharmaceutical tools must be approached as a late-stage translational concern rather than as a direct consequence of discovery performance. In clinical settings, AI is most appropriately framed as an assistive layer that may help organise evidence, clarify uncertainty, and support expert review, while responsibility for interpretation and patient-centred decision-making remains with qualified professionals. Human-centred AI in medicine emphasises augmentation rather than replacement, which is particularly important for phytopharmaceutical translation because product identity, safety context, concomitant medicine use, and claim boundaries require professional judgement [25].

A major adoption barrier is the gap between model performance and clinical usefulness. Even when AI models perform well in development or benchmark environments, they may fail to deliver clinical impact if they are not externally validated, do not fit workflow constraints, provide unclear explanations, or create cognitive burden for clinicians. For AI-enabled phytopharmaceutical translation, workflow fit must therefore include usability, documentation, uncertainty communication, safety review, interaction checking, and clear indication that the system supports evidence interpretation rather than autonomous therapeutic recommendation [26].

Clinical trust also depends on transparency, replicability, ethics, and effectiveness evidence. Patient-benefit AI requires that users understand what data were used, how

outputs should be interpreted, what limitations remain, and what safeguards are in place when uncertainty is high [27]. Early-stage AI decision-support evaluation further reinforces the need to assess human interaction, intended use, clinical context, and workflow consequences before any routine use is considered [28]. In phytopharmaceutical translation, such evaluation should include whether clinicians can distinguish discovery-stage predictions from validated evidence, whether safety warnings are understandable, and whether model uncertainty is visible at the point of interpretation.

Responsible clinical adoption further requires safeguards across design, evaluation, implementation, and monitoring. A do-no-harm approach to machine learning in health care highlights the need for risk assessment, monitoring, stakeholder engagement, and post-deployment review [29]. Governance models for healthcare AI also emphasise accountability, oversight, safety, and institutional responsibility, which are essential when AI outputs may influence interpretation of phytopharmaceutical evidence [30]. More broadly, clinical AI adoption depends on integration into real clinical contexts, protection against automation bias, and alignment with human oversight, rather than assuming that computational sophistication alone will produce safe or useful adoption [31].

Figure 1 illustrates clinical adoption pathways for AI-enabled phytopharmaceutical translation, connecting workflow readiness, human oversight, patient safety, explainability, implementation monitoring, and adoption boundaries.

Figure 1. Clinical Adoption Pathways for AI-Enabled Phytopharmaceutical Translation

Alt-text description

A conceptual pathway diagram showing validated phytopharmaceutical evidence and AI outputs moving through clinical workflow fit, explainability, human oversight, clinician trust, patient safety, pharmacovigilance readiness, implementation monitoring, and adoption boundaries.

Table 3 summarises clinical adoption pathway requirements for AI-enabled phytopharmaceutical translation.

Table 3. Clinical Adoption Pathways for AI-Enabled Phytopharmaceutical Translation: Clinical Workflow Fit, Human Oversight, Clinician Trust, Patient Safety, Explainability, Pharmacovigilance Readiness, Implementation Monitoring, and Adoption Boundaries

Adoption domain	Core adoption question	Stakeholder involved	Evidence or workflow requirement	Barrier	Safeguard	Validation boundary	Roadmap implication
Clinical workflow fit	Can the tool fit real clinical processes?	Clinicians, informaticians, implementation teams	Workflow mapping, usability review, documentation pathway	Disruption, alert fatigue, unclear role	Human factors review and workflow testing	Workflow fit does not prove clinical benefit	Adoption planning must begin before deployment
Human oversight	Who reviews and acts on AI outputs?	Clinicians, pharmacologists, safety reviewers	Defined expert-review and escalation roles	Automation bias or unclear responsibility	Human-in-the-loop review	Oversight does not guarantee correctness	Clinical use must remain bounded by professional judgement

Clinician trust	Can clinicians understand and appropriately use outputs?	Clinicians, educators, developers	Transparent evidence summaries, uncertainty statements, training	Distrust, overtrust, limited interpretability	Trust calibration and training	Trust is not proof of efficacy	Trust-building must be evidence-informed
Patient safety	How are patients protected from unsafe interpretation?	Clinicians, patients, safety teams	Contraindication, interaction, adverse-event, and exposure review	Hidden toxicity or interaction risks	Patient-safety escalation pathway	Safety screening is not safety assurance	Safety evidence must precede adoption claims
Explainability	Are outputs interpretable enough for review?	Developers, clinicians, pharmacologists	Feature, target, pathway, and evidence explanations	Black-box output or misleading explanation	Explanation quality audit	Explanation is not experimental validation	Explainability supports review, not proof
Pharmacovigilance readiness	Can safety signals be monitored after use?	Pharmacovigilance teams, clinicians, regulators	Signal detection, adverse-event capture, exposure context	Underreporting and causality uncertainty	Signal review and escalation governance	Readiness is not evidence of safety	Monitoring must be built into lifecycle planning
Implementation monitoring	Can performance and safety be watched over time?	Health systems, quality teams, developers	Drift monitoring, audit logs, safety review, update triggers	Silent degradation	Periodic monitoring and revalidation	Monitoring cannot compensate for weak validation	Adoption requires lifecycle oversight
Decision-support boundary	What should the tool not do?	Clinicians, institutions, developers, regulators	Intended-use statement, no autonomous treatment instruction, claim boundaries	Misuse or therapeutic overreach	Boundary documentation and user training	Boundary setting does not establish utility	Adoption requires explicit limits
Stakeholder engagement	Are relevant users involved in translation planning?	Clinicians, patients, researchers, regulators, developers	Participatory review, usability input, safety concerns	Poor acceptance or overlooked risks	Multistakeholder governance	Engagement is not validation	Roadmap must include trust and acceptability
Accountability	Who is responsible for errors, updates, and decisions?	Institutions, clinicians, developers, governance boards	Responsibility map, audit trail, escalation rules	Diffuse responsibility	Accountability register	Accountability planning is not legal certification	Governance must accompany technical development

Strategic roadmap

The proposed strategic roadmap begins with data infrastructure and proceeds through model validation, mechanistic evidence, safety integration, regulatory alignment, clinical adoption planning, monitored implementation, and continuous learning. Its logic is that model performance becomes translationally meaningful only when connected to clinical usefulness, evidence quality, and responsible implementation conditions. Machine learning in medicine has shown that predictive accuracy alone is insufficient unless models are generalisable, interpretable within context, and linked to real decision pathways [32].

The second roadmap layer concerns ethical implementation and governance. AI-enabled phytopharmaceutical translation requires explicit attention to who curates the data, who reviews the model output, who defines intended use, who monitors safety, and who remains accountable when uncertainty is high. Ethical implementation of machine learning in health care highlights the importance of aligning technical development with patient protection, accountability, and institutional responsibility [33]. In this roadmap, governance is not a final administrative step; it is a continuous control layer that begins with data provenance and continues through model updating and post-adoption monitoring.

The third roadmap layer is transparent reporting. Minimum information standards for clinical AI modelling support reproducibility by requiring clear description of data sources, modelling choices, validation procedures, intended use, and limitations [34]. For AI-enabled phytopharmaceutical translation, analogous documentation should capture natural product identity, chemical annotation confidence, assay context, model version, training data provenance, external validation

status, safety evidence, uncertainty, and claim boundaries. Such reporting does not validate a tool by itself, but it enables independent review and prevents unsupported movement from discovery-stage prediction to clinical interpretation.

The fourth roadmap layer is realism about AI drug-discovery maturity. Strategic translation should avoid assuming that improved algorithms automatically resolve data sparsity, chemical novelty, biological complexity, safety uncertainty, or experimental reproducibility. Contemporary appraisal of AI for drug discovery emphasises that the field still faces major challenges in validation, data quality, and translation beyond benchmark performance [35]. For phytopharmaceuticals, these challenges are amplified by heterogeneous product definitions, multi-component preparations, traditional-use evidence, and complex safety contexts.

The fifth roadmap layer is risk governance. Bias mitigation, fairness review, accountability, and safety assurance must be embedded within the roadmap rather than treated as optional add-ons after technical development. Accountability and safety scholarship in healthcare AI further indicates that responsibility must be distributed clearly across developers, institutions, clinicians, and governance bodies when AI systems influence health-related interpretation [36]. The proposed roadmap therefore treats each stage as an evidence gate: progression is justified only when data readiness, validation credibility, mechanism plausibility, safety interpretation, regulatory claim boundaries, workflow fit, and oversight requirements are sufficiently addressed for the intended purpose.

Table 4 presents the proposed strategic roadmap for AI-enabled phytopharmaceutical translation.

Table 4. Proposed Strategic Roadmap for AI-Enabled Phytopharmaceutical Translation: Data Infrastructure, Model Validation, Mechanistic Evidence, Safety Integration, Regulatory Alignment, Clinical Adoption Planning, Governance, Continuous Learning, and Future Evidence Updating

Roadmap stage	Core objective	Required input	Key action	Evidence gate	Governance safeguard	Expected strategic output	Failure risk	Next-stage requirement
Data infrastructure	Establish reusable, traceable evidence	FAIR chemical, biological, safety, omics, clinical, and traditional-use data where relevant	Curate, standardise, version, and link evidence	Data provenance and interoperability audit	Data governance and metadata stewardship	Translation-ready evidence base	Fragmented or ambiguous data	Chemical and biological readiness review
Natural product identity	Define the entity under evaluation	Compound, extract, fraction, formulation, source, preparation metadata	Resolve identity and annotation confidence	Identity confirmation	Source documentation and curation control	Clearly bounded phytopharmaceutical entity	Treating non-equivalent materials as equivalent	Model-input preparation
Model development	Generate computational hypotheses	Curated training data, features, task definition, model documentation	Train models for defined discovery or evidence-integration tasks	Internal validation	Transparent model documentation	Hypothesis-generating AI output	Overfitting or leakage	External validation
Model validation	Assess credibility and generalisability	Independent datasets, benchmarks, calibration, uncertainty estimates	Conduct external testing and applicability-domain assessment	External validation and uncertainty review	Independent methodological review	Credible but bounded model output	Poor generalisability	Mechanistic evidence generation
Mechanistic evidence	Test biological plausibility	Target, pathway, omics, network, and experimental evidence	Map and validate mechanism hypotheses	Mechanistic plausibility and experimental support	Claim-boundary control	Evidence-supported mechanism hypothesis	Network or omics overinterpretation	Safety integration

Safety integration	Identify and manage risk	ADMET, toxicity, interaction, pharmacovigilance, exposure evidence	Integrate safety evidence and uncertainty	Safety-risk review	Safety escalation and monitoring plan	Safety-aware translation profile	Missed toxicity or interaction risk	Regulatory alignment
Regulatory alignment	Match evidence to intended claims	Validation, safety, mechanism, documentation, intended-use statement	Define claim boundaries and evidence requirements	Evidence-to-claim audit	Regulatory interpretation governance	Regulatory-aligned evidence dossier	Implying approval or unsupported claims	Clinical adoption planning
Clinical adoption planning	Assess workflow and decision-support role	Clinical pathway, user needs, safety procedures, explainability	Define workflow fit, oversight, and usability requirements	Workflow-readiness review	Human oversight and accountability plan	Adoption-planning framework	Workflow burden or automation bias	Monitored implementation planning
Monitored implementation	Evaluate use under controlled conditions where appropriate	Governance plan, monitoring metrics, safety procedures, feedback pathways	Monitor performance, safety, drift, and user interpretation	Monitoring and revalidation review	Auditability and escalation governance	Controlled learning environment	Silent model degradation	Continuous learning
Continuous learning	Update evidence and models responsibly	New evidence, post-adoption signals, model updates, stakeholder feedback	Reassess data, claims, models, and safeguards	Revalidation after updates	Change-control governance	Updated evidence and roadmap refinement	Uncontrolled updates	Renewed lifecycle review

Figure 2 presents the proposed strategic roadmap for AI-enabled phytopharmaceutical translation across data infrastructure, model validation, mechanistic evidence, regulatory alignment, clinical adoption, governance, and continuous learning.

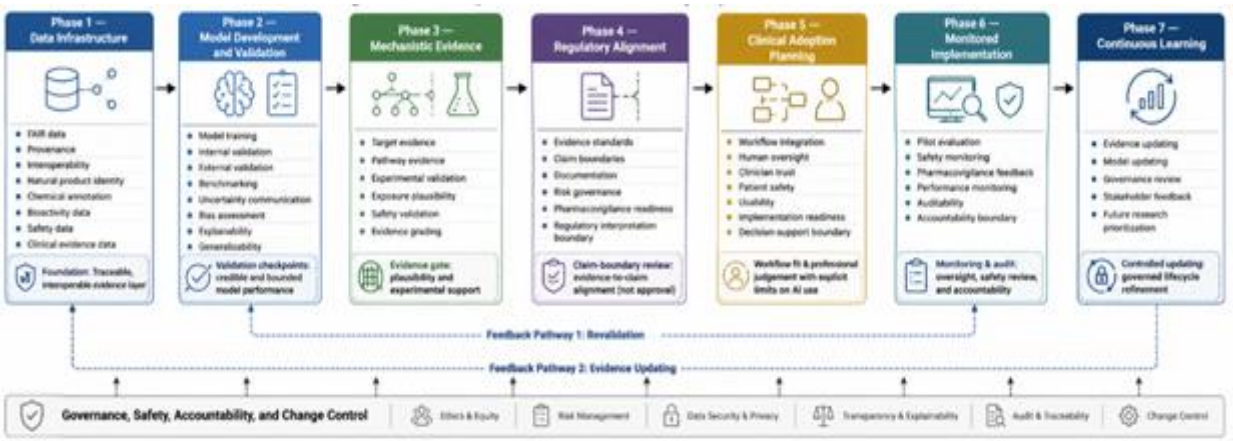

Figure 2. Strategic Roadmap for AI-Enabled Phytopharmaceutical Translation

Alt-text description

A staged strategic roadmap showing AI-enabled phytopharmaceutical translation from data infrastructure and model validation through mechanistic evidence, safety integration, regulatory alignment, clinical adoption planning, governance, monitoring, and continuous learning.

Future research priorities

A major future priority is the creation of interoperable, multimodal phytopharmaceutical evidence systems that connect chemical identity, biosynthetic context, omics profiles, bioactivity, safety, traditional-use context where relevant, and clinical evidence. Knowledge graphs and

multimodal AI approaches may help natural product science organise heterogeneous evidence and support more transparent inference, but their translational value will depend on curation quality, evidence grading, uncertainty representation, and mechanisms for updating records as new data emerge [37].

Future work should also strengthen natural product databases by improving standardised identifiers, source traceability, chemical annotation confidence, assay metadata, and links between compounds, extracts, species, targets, pathways, safety records, and clinical evidence. Database development for natural product drug discovery can support AI-enabled translation only when records are interoperable, provenance-aware, and sufficiently detailed to distinguish hypothesis-generating evidence from validated pharmacological or clinical evidence [38]. This priority is especially important for phytopharmaceuticals because unresolved identity and inconsistent annotation can undermine model training, external validation, and claim-boundary definition.

A further research priority is the development of validation protocols that reflect real translational risks. Future AI-enabled phytopharmaceutical studies should move beyond internal performance metrics toward external validation, prospective evaluation where appropriate, uncertainty calibration, bias assessment, safety-aware prediction, experimental confirmation, and workflow-oriented evaluation. The future of machine learning for small-molecule discovery is likely to be constrained by data quality, accessibility, and evaluation design, making benchmark phytopharmaceutical datasets, external validation frameworks, explainability standards, pharmacovigilance integration, and governance models essential for responsible translation.

CONCLUSION

AI-enabled phytopharmaceutical translation requires a staged strategic roadmap rather than reliance on predictive outputs alone. The roadmap proposed in this article integrates data infrastructure, natural product identity, model validation, mechanistic evidence, safety interpretation, regulatory alignment, clinical adoption planning, human oversight, governance safeguards, implementation monitoring, and continuous evidence updating. Its central contribution is to define how computational discovery can support responsible translation planning while preserving clear distinctions between hypothesis generation, validation, mechanistic plausibility, safety evidence, regulatory interpretation, workflow readiness, and clinical adoption. Responsible translation will depend on evidence development, validation, safety safeguards, clinical workflow alignment, stakeholder trust, and continuous governance.

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